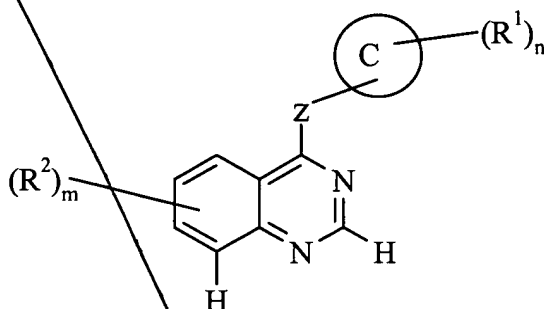


IN THE CLAIMS:

Please amend claims 1-3, 6-14 and 16-17 to read as follows:

1. (Amended) A method for producing an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal in need thereof, which comprises administering to said animal an effective amount of a compound of the formula I:



(I)

wherein:

ring C is a 5-6-membered heterocyclic moiety which may be saturated or unsaturated, which may be aromatic or non-aromatic, and which contains 1-3 heteroatoms selected independently from O, N and S;

Z is -O-, -NH-, -S- or -CH₂-;

R¹ represents hydrogen, C₁₋₄alkyl, C₁₋₄alkoxymethyl, di(C₁₋₄alkoxy)methyl, C₁₋₄alkanoyl, trifluoromethyl, cyano, amino, C₂₋₅alkenyl, C₂₋₅alkynyl, a phenyl group, a benzyl group or a 5-6-membered heterocyclic group with 1-3 heteroatoms, selected independently from O, S and N, which heterocyclic group may be aromatic or non-aromatic and may be saturated (linked via a ring carbon or nitrogen atom) or unsaturated (linked via a ring carbon atom), and which phenyl, benzyl or heterocyclic group may bear on one or more ring carbon atoms up to 5 substituents selected from hydroxy, halogeno, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃alkanoyloxy, trifluoromethyl, cyano, amino, nitro, C₂₋₄alkanoyl, C₁₋₄alkanoylamino, C₁₋₄alkoxycarbonyl, C₁₋₄alkylsulphanyl, C₁₋₄alkylsulphinyl,

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C₁₋₄alkylsulphonyl, carbamoyl, N-C₁₋₄alkylcarbamoyl, N,N-di(C₁₋₄alkyl)carbamoyl, aminosulphonyl, N-C₁₋₄alkylaminosulphonyl, N,N-di(C₁₋₄alkyl)aminosulphonyl, C₁₋₄alkylsulphonylamino, C₁₋₄alkylamino, C₁₋₄hydroxyalkyl, C₁₋₄aminoalkyl, C₁₋₄haloalkyl, C₁₋₄hydroxyalkoxy, carboxy and a saturated heterocyclic group selected from morpholino, thiomorpholino, pyrrolidinyl, piperazinyl, piperidinyl, imidazolidinyl and pyrazolidinyl, which saturated heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃alkanoyloxy, trifluoromethyl, cyano, amino, nitro and C₁₋₄alkoxycarbonyl; and additionally R¹ may represent carboxy, C₃₋₇cycloalkyl, C₃₋₇cycloalkylC₁₋₃alkyl, or phenylC₂₋₄alkyl wherein the phenyl moiety may bear up to 5 substituents selected from the list herein defined for a phenyl ring which is directly linked to ring C;

n is an integer from 0 to 5;

m is an integer from 0 to 3;

R² represents hydrogen, hydroxy, halogeno, cyano, nitro, trifluoromethyl, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃alkylsulphonyl, -NR³R⁴ (wherein R³ and R⁴, which may be the same or different, each represents hydrogen or C₁₋₃alkyl), or R⁵X¹- (wherein X¹ represents a direct bond, -O-, -CH₂-, -OCO-, carbonyl, -S-, -SO-, -SO₂-, -NR⁶CO-, -CONR⁷-, -SO₂NR⁸-, -NR⁹SO₂- or -NR¹⁰- (wherein R⁶, R⁷, R⁸, R⁹ and R¹⁰ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl), and R⁵ is selected from one of the following eighteen groups:

- 1) hydrogen or C₁₋₅alkyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, fluoro, chloro, bromo and amino;
- 2) C₁₋₅alkylX²COR¹¹ (wherein X² represents -O- or -NR¹²- (in which R¹² represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R¹¹ represents C₁₋₃alkyl, -NR¹³R¹⁴ or -OR¹⁵ (wherein R¹³, R¹⁴ and R¹⁵ which may be the same or different each represents hydrogen, C₁₋₃alkyl, C₄₋₅alkyl or C₁₋₃alkoxyC₂₋₃alkyl));
- 3) C₁₋₅alkylX³R¹⁶ (wherein X³ represents -O-, -S-, -SO-, -SO₂-, -OCO-, -NR¹⁷CO-, -CONR¹⁸-, -SO₂NR¹⁹-, -NR²⁰SO₂- or -NR²¹- (wherein R¹⁷, R¹⁸, R¹⁹, R²⁰ and R²¹ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R¹⁶

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represents hydrogen, C₁₋₃alkyl, cyclopentyl, cyclohexyl or a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C₁₋₃alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and C₁₋₄alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₄alkyl, C₁₋₄hydroxyalkyl, C₁₋₄alkoxy, C₁₋₄cyanoalkyl and C₁₋₄alkoxycarbonyl);

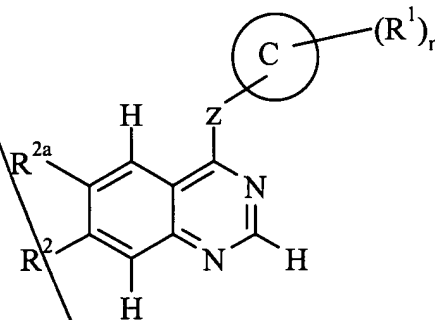
- 4) C₁₋₅alkylX⁴C₁₋₅alkylX⁵R²² (wherein X⁴ and X⁵ which may be the same or different are each -O-, -S-, -SO-, -SO₂-, -NR²³CO-, -CONR²⁴-, -SO₂NR²⁵-, -NR²⁶SO₂- or -NR²⁷- (wherein R²³, R²⁴, R²⁵, R²⁶ and R²⁷ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R²² represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl);
- 5) R²⁸ (wherein R²⁸ is a 5-6-membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₄alkyl, C₁₋₄hydroxyalkyl, C₁₋₄alkoxy, C₁₋₄alkoxyC₁₋₄alkyl, C₁₋₄alkylsulphonylC₁₋₄alkyl and C₁₋₄alkoxycarbonyl);
- 6) C₁₋₅alkylR²⁸ (wherein R²⁸ is as defined herein);
- 7) C₂₋₅alkenylR²⁸ (wherein R²⁸ is as defined herein);
- 8) C₂₋₅alkynylR²⁸ (wherein R²⁸ is as defined herein);
- 9) R²⁹ (wherein R²⁹ represents a pyridone group, a phenyl group or a 5-6-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-3 heteroatoms selected from O, N and S, which pyridone, phenyl or aromatic heterocyclic group may carry up to 5 substituents on an available carbon atom selected from hydroxy, halogeno, amino, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄hydroxyalkyl, C₁₋₄aminoalkyl, C₁₋₄alkylamino, C₁₋₄hydroxyalkoxy, carboxy, trifluoromethyl, cyano, -CONR³⁰R³¹ and -NR³²COR³³ (wherein R³⁰, R³¹, R³² and R³³, which may be the same or different, each represents hydrogen, C₁₋₄alkyl or C₁₋₃alkoxyC₂₋₃alkyl));
- 10) C₁₋₅alkylR²⁹ (wherein R²⁹ is as defined herein);
- 11) C₂₋₅alkenylR²⁹ (wherein R²⁹ is as defined herein);

- Sub
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- 12) C₂₋₅alkynylR²⁹ (wherein R²⁹ is as defined herein);
- 13) C₁₋₅alkylX⁶R²⁹ (wherein X⁶ represents -O-, -S-, -SO-, -SO₂-, -NR³⁴CO-, -CONR³⁵-, -SO₂NR³⁶-, -NR³⁷SO₂- or -NR³⁸- (wherein R³⁴, R³⁵, R³⁶, R³⁷ and R³⁸ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R²⁹ is as defined herein);
- 14) C₂₋₅alkenylX⁷R²⁹ (wherein X⁷ represents -O-, -S-, -SO-, -SO₂-, -NR³⁹CO-, -CONR⁴⁰-, -SO₂NR⁴¹-, -NR⁴²SO₂- or -NR⁴³- (wherein R³⁹, R⁴⁰, R⁴¹, R⁴² and R⁴³ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R²⁹ is as defined herein);
- 15) C₂₋₅alkynylX⁸R²⁹ (wherein X⁸ represents -O-, -S-, -SO-, -SO₂-, -NR⁴⁴CO-, -CONR⁴⁵-, -SO₂NR⁴⁶-, -NR⁴⁷SO₂- or -NR⁴⁸- (wherein R⁴⁴, R⁴⁵, R⁴⁶, R⁴⁷ and R⁴⁸ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R²⁹ is as defined herein);
- 16) C₁₋₃alkylX⁹C₁₋₃alkylR²⁹ (wherein X⁹ represents -O-, -S-, -SO-, -SO₂-, -NR⁴⁹CO-, -CONR⁵⁰-, -SO₂NR⁵¹-, -NR⁵²SO₂- or -NR⁵³- (wherein R⁴⁹, R⁵⁰, R⁵¹, R⁵² and R⁵³ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R²⁹ is as defined herein);
- 17) C₁₋₃alkylX⁹C₁₋₃alkylR²⁸ (wherein X⁹ and R²⁸ are as defined herein); and
- 18) C₁₋₃alkylR⁵⁴C₁₋₃alkylX⁹R⁵⁵ (wherein X⁹ is as defined herein and R⁵⁴ and R⁵⁵ are each independently selected from hydrogen, C₁₋₃alkyl, cyclopentyl, cyclohexyl and a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C₁₋₃alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and C₁₋₄alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₄alkyl, C₁₋₄hydroxyalkyl, C₁₋₄alkoxy, C₁₋₄cyanoalkyl and C₁₋₄alkoxycarbonyl), with the proviso that R⁵⁴ cannot be hydrogen;

and additionally wherein any C₁₋₅alkyl, C₂₋₅alkenyl or C₂₋₅alkynyl group in R⁵X¹- may bear one or more substituents selected from hydroxy, halogeno and amino;

or a pharmaceutically acceptable salt thereof.

2. (Amended) A method for producing an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal in need thereof, which comprises administering to said animal an effective amount of a compound of the formula Ia:

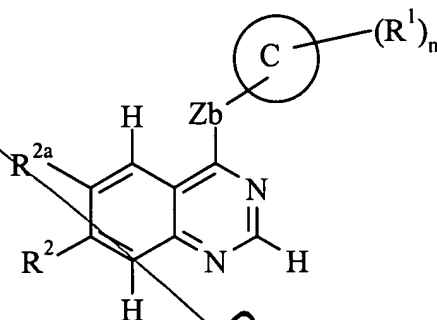


(Ia)

wherein:

ring C , R^1 , R^2 , n and Z are as defined in claim 1 with the proviso that R^2 is not hydrogen; and R^{2a} represents hydrogen, halogeno, C_{1-3} alkyl, C_{1-3} alkoxy, C_{1-3} alkylthio, $-NR^{3a}R^{4a}$ (wherein R^{3a} and R^{4a} , which may be the same or different, each represents hydrogen or C_{1-3} alkyl), or $R^{5a}(CH_2)_{za}X^{1a}$ (wherein R^{5a} is a 5- or 6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-4} alkyl, C_{1-4} hydroxyalkyl and C_{1-4} alkoxy, za is an integer from 0 to 4 and X^{1a} represents a direct bond, $-O-$, $-CH_2-$, $-S-$, $-SO-$, $-SO_2-$, $-NR^{6a}CO-$, $-CONR^{7a}-$, $-SO_2NR^{8a}-$, $-NR^{9a}SO_2-$ or $-NR^{10a}-$ (wherein R^{6a} , R^{7a} , R^{8a} , R^{9a} and R^{10a} each independently represents hydrogen, C_{1-3} alkyl or C_{1-3} alkoxy C_{2-3} alkyl)); or a pharmaceutically acceptable salt thereof.

3. (Amended) A method for producing an antiangiogenic or vascular permeability reducing effect in a warm-blooded animal in need thereof, which comprises administering to said animal an effective amount of a compound of the formula Ib:



(Ib)

wherein:

ring C , R^1 , R^2 and n are as defined in claim 1 with the proviso that R^2 is not hydrogen, R^{2a} is as defined in claim 2; and

Zb is $-O-$ or $-S-$;

or a pharmaceutically acceptable salt thereof.

5. (Amended) A compound as claimed in claim 18 wherein Zb is $-O-$.

6. (Amended) A compound as claimed in claim 18 wherein R^{2a} is methoxy.

7. (Amended) A compound as claimed in claim 18 wherein ring C is a 5-membered heteroaromatic moiety which contains 1-3 heteroatoms selected independently from O, N and S.

8. (Amended) A compound as claimed in claim 18 wherein R^1 is a phenyl group or a 5-6-membered heteroaromatic group with 1-3 heteroatoms, selected independently from O, S and N, (linked via a ring carbon atom), which phenyl or heteroaromatic group is optionally substituted as defined in claim 18.

9. (Amended) A compound as claimed in claim 18 wherein

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 R^2 represents hydroxy, halogeno, nitro, trifluoromethyl, C_{1-3} alkyl, cyano, amino or R^5X^1 - wherein X^1 is as defined in claim 18 and R^5 is selected from one of the following eighteen groups:

- 1) C_{1-4} alkyl which may be unsubstituted or substituted with one or more fluorine atoms, or C_{2-4} alkyl which may be unsubstituted or substituted with 1 or 2 groups selected from hydroxy and amino;
- 2) $C_{2-3}alkylX^2COR^{11}$ (wherein X^2 is as defined in claim 18 and R^{11} represents $-NR^{13}R^{14}$ or $-OR^{15}$ (wherein R^{13} , R^{14} and R^{15} which may be the same or different are each C_{1-2} alkyl or $C_{1-2}alkoxyethyl$));
- 3) $C_{2-4}alkylX^3R^{16}$ (wherein X^3 is as defined in claim 18 and R^{16} is a group selected from C_{1-3} alkyl, cyclopentyl, cyclohexyl, pyrrolidinyl and piperidinyl which group is linked to X^3 through a carbon atom and which C_{1-3} alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and $C_{1-2}alkoxy$ and which cyclopentyl, cyclohexyl, pyrrolidinyl or piperidinyl group may carry one substituent selected from oxo, hydroxy, halogeno, C_{1-2} alkyl, $C_{1-2}hydroxyalkyl$ and $C_{1-2}alkoxy$);
- 4) $C_{2-3}alkylX^4C_{2-3}alkylX^5R^{22}$ (wherein X^4 and X^5 are as defined in claim 18 and R^{22} represents hydrogen or C_{1-3} alkyl);
- 5) $C_{1-4}alkylR^{59}$ (wherein R^{59} is a group selected from pyrrolidinyl, piperazinyl, piperidinyl, 1,3-dioxolan-2-yl, 1,3-dioxan-2-yl, 1,3-dithiolan-2-yl and 1,3-dithian-2-yl, which group is linked to $C_{1-4}alkyl$ through a carbon atom and which group may carry 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-3} alkyl, $C_{1-3}hydroxyalkyl$, $C_{1-3}alkoxy$, $C_{1-2}alkoxyC_{1-3}alkyl$ and $C_{1-2}alkylsulphonylC_{1-3}alkyl$) or $C_{2-4}alkylR^{60}$ (wherein R^{60} is a group selected from morpholino, thiomorpholino, pyrrolidin-1-yl, piperazin-1-yl and piperidino which group may carry 1 or 2 substituents selected from oxo, hydroxy, halogeno, C_{1-3} alkyl, $C_{1-3}hydroxyalkyl$, $C_{1-3}alkoxy$, $C_{1-2}alkoxyC_{1-3}alkyl$ and $C_{1-2}alkylsulphonylC_{1-3}alkyl$);
- 6) $C_{3-4}alkenylR^{61}$ (wherein R^{61} represents R^{59} or R^{60} as defined herein);
- 7) $C_{3-4}alkynylR^{61}$ (wherein R^{61} represents R^{59} or R^{60} as defined herein);
- 8) R^{29} (wherein R^{29} is as defined in claim 18);

- 9) C₁₋₄alkylR²⁹ (wherein R²⁹ is as defined in claim 18);
- 10) 1-R²⁹prop-1-en-3-yl or 1-R²⁹but-2-en-4-yl (wherein R²⁹ is as defined in claim 18 with the proviso that when R⁵ is 1-R²⁹prop-1-en-3-yl, R²⁹ is linked to the alkenyl group via a carbon atom);
- 11) 1-R²⁹prop-1-yn-3-yl or 1-R²⁹but-2-yn-4-yl (wherein R²⁹ is as defined in claim 18 with the proviso that when R⁵ is 1-R²⁹prop-1-yn-3-yl, R²⁹ is linked to the alkynyl group via a carbon atom);
- 12) C₁₋₅alkylX⁶R²⁹ (wherein X⁶ and R²⁹ are as defined in claim 18);
- 13) 1-(R²⁹X⁷)but-2-en-4-yl (wherein X⁷ and R²⁹ are as defined in claim 18);
- 14) 1-(R²⁹X⁸)but-2-yn-4-yl (wherein X⁸ and R²⁹ are as defined in claim 18);
- 15) C₂₋₃alkylX⁹C₁₋₂alkylR²⁹ (wherein X⁹ and R²⁹ are as defined in claim 18);
- 16) R²⁸ (wherein R²⁸ is as defined in claim 18);
- 17) C₂₋₃alkylX⁹C₁₋₂alkylR²⁸ (wherein X⁹ and R²⁸ are as defined in claim 18); and
- 18) C₂₋₃alkylR⁵⁴C₁₋₂alkylX⁹R⁵⁵ (wherein X⁹, R⁵⁴ and R⁵⁵ are as defined in claim 18);
- and additionally wherein any C₁₋₅alkyl, C₂₋₅alkenyl or C₂₋₅alkynyl group in R⁵X¹- may bear one or more substituents selected from hydroxy, halogeno and amino.

10. (Amended) A compound as claimed in claim 18 wherein R² represents

2-methoxyethoxy, 2-(2-methoxyethoxy)ethoxy, 3-methoxypropoxy,

2-methylsulphonylethoxy, 3-methylsulphonylpropoxy, 2-(tetrahydropyran-4-yloxy)ethoxy,

3-(tetrahydropyran-4-yloxy)propoxy, 2-(4-methylpiperazin-1-yl)ethoxy,

3-(4-methylpiperazin-1-yl)propoxy, 2-morpholinoethoxy, 3-morpholinopropoxy,

2-(imidazol-1-yl)ethoxy, 3-(imidazol-1-yl)propoxy 2-(1,1-dioxothiomorpholino)ethoxy,

3-(1,1-dioxothiomorpholino)propoxy, 2-(1,2,3-triazol-1-yl)ethoxy,

3-(1,2,3-triazol-1-yl)propoxy, 2-(N-methoxyacetyl-N-methylamino)ethoxy,

3-(N-methoxyacetyl-N-methylamino)propoxy, N-methylpiperidin-3-ylmethoxy,

4-(pyrrolidin-1-yl)but-2-en-yloxy, 2-(2-oxopyrrolidin-1-yl)ethoxy,

3-(2-oxopyrrolidin-1-yl)propoxy, 2-(pyrrolidin-1-yl)ethoxy, 3-(pyrrolidin-1-yl)propoxy,

2-(2-(pyrrolidin-1-yl)ethoxy)ethoxy, 2-(2-(4-methylpiperazin-1-yl)ethoxy)ethoxy,

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2-piperidinoethoxy, 3-piperidinopropoxy, 2-(methylpiperidino)ethoxy,
3-(methylpiperidino)propoxy, 2-(ethylpiperidino)ethoxy, 3-(ethylpiperidino)propoxy,
2-((2-methoxyethyl)piperidino)ethoxy, 3-((2-methoxyethyl)piperidino)propoxy,
2-((2-methylsulphonyl)ethylpiperidino)ethoxy,
3-((2-methylsulphonyl)ethylpiperidino)propoxy, piperidin-3-ylmethoxy,
piperidin-4-ylmethoxy, 2-(piperidin-3-yl)ethoxy, 2-(piperidin-4-yl)ethoxy,
3-(piperidin-3-yl)propoxy, 3-(piperidin-4-yl)propoxy, 2-(methylpiperidin-3-yl)ethoxy,
2-(methylpiperidin-4-yl)ethoxy, 3-(methylpiperidin-3-yl)propoxy,
3-(methylpiperidin-4-yl)propoxy, 2-(ethylpiperidin-3-yl)ethoxy,
2-(ethylpiperidin-4-yl)ethoxy, 3-(ethylpiperidin-3-yl)propoxy,
3-(ethylpiperidin-4-yl)propoxy, 2-((2-methoxyethyl)piperidin-3-yl)ethoxy,
2-((2-methoxyethyl)piperidin-4-yl)ethoxy, 3-((2-methoxyethyl)piperidin-3-yl)propoxy,
3-((2-methoxyethyl)piperidin-4-yl)propoxy,
2-((2-methylsulphonylethyl)piperidin-3-yl)ethoxy,
2-((2-methylsulphonylethyl)piperidin-4-yl)ethoxy,
3-((2-methylsulphonylethyl)piperidin-3-yl)propoxy,
3-((2-methylsulphonylethyl)piperidin-4-yl)propoxy, 1-isopropylpiperidin-2-ylmethyl,
1-isopropylpiperidin-3-ylmethyl, 1-isopropylpiperidin-4-ylmethyl,
2-(1-isopropylpiperidin-2-yl)ethyl, 2-(1-isopropylpiperidin-3-yl)ethyl,
2-(1-isopropylpiperidin-4-yl)ethyl, 3-(1-isopropylpiperidin-2-yl)propyl,
3-(1-isopropylpiperidin-3-yl)propyl, 3-(1-isopropylpiperidin-4-yl)propyl,
3-(4-methylpiperazin-1-yl)propoxy, 1-methylpiperidin-4-ylmethoxy,
1-(2-methylsulphonylethyl)piperidin-4-ylmethoxy,
1-(2-pyrrolidinylethyl)piperidin-4-ylmethoxy,
1-(3-pyrrolidinylpropyl)piperidin-4-ylmethoxy, 1-(2-piperidinylethyl)piperidin-4-ylmethoxy,
1-(3-piperidinylpropyl)piperidin-4-ylmethoxy, 1-(2-morpholinoethyl)piperidin-4-ylmethoxy,
1-(3-morpholinopropyl)piperidin-4-ylmethoxy,
1-(2-thiomorpholinoethyl)piperidin-4-ylmethoxy,

1-(3-thiomorpholinopropyl)piperidin-4-ylmethoxy,
1-(2-azetidinyethyl)piperidin-4-ylmethoxy or 1-(3-azetidinypropyl)piperidin-4-ylmethoxy.

11. (Amended) A compound as claimed in claim 18 selected from:

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4-(5-(4-methoxyphenyl)pyrazol-3-yloxy)-6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)-quinazoline,
4-(5-(4-methoxyphenyl)pyrazol-3-yloxy)-6-methoxy-7-(3-(4-methylpiperazin-1-yl)-propoxy)quinazoline,
6-methoxy-7-(2-(2-methoxyethoxy)ethoxy)-4-(5-phenylpyrazol-3-yloxy)quinazoline,
4-(5-(3-furyl)pyrazol-3-yloxy)-6-methoxy-7-(3-morpholinopropoxy)quinazoline,
6-methoxy-7-(3-morpholinopropoxy)-4-(5-phenylpyrazol-3-yloxy)quinazoline,
7-(2-(imidazol-1-yl)ethoxy)-6-methoxy-4-(5-phenylpyrazol-3-yloxy)quinazoline,
4-(5-(4-chlorophenyl)pyrazol-3-yloxy)-6-methoxy-7-(3-morpholinopropoxy)quinazoline,
6-methoxy-7-(3-(4-methylpiperazin-1-yl)propoxy)-4-(5-phenylpyrazol-3-yloxy)-quinazoline,
6-methoxy-7-(2-methoxyethoxy)-4-(5-phenylpyrazol-3-yloxy)quinazoline,
4-(5-(4-methoxyphenyl)pyrazol-3-yloxy)-6-methoxy-7-(2-(1,2,3-triazol-1-yl)ethoxy)-quinazoline and
4-(5-(4-methoxyphenyl)pyrazol-3-yloxy)-6-methoxy-7-(1-(2-methylsulphonyl)ethyl)-piperidin-4-ylmethoxy)quinazoline,
and salts thereof.

12. (Amended) A compound as claimed in claim 18 selected from:

7-(2-methoxyethoxy)-4-(5-phenylpyrazol-3-yloxy)quinazoline,
4-(5-(2-fluorophenyl)pyrazol-3-yloxy)-6-methoxy-7-(3-morpholinopropoxy)quinazoline,
6-methoxy-7-(3-morpholinopropoxy)-4-(5-(3-nitrophenyl)pyrazol-3-yloxy)quinazoline,
6-methoxy-7-(3-morpholinopropoxy)-4-(5-(4-nitrophenyl)pyrazol-3-yloxy)quinazoline,
6-methoxy-7-(3-morpholinopropoxy)-4-(5-(4-pyridyl)pyrazol-3-yloxy)quinazoline,
4-(5-(4-fluorophenyl)pyrazol-3-yloxy)-6-methoxy-7-(3-morpholinopropoxy)quinazoline, and
6-methoxy-7-(2-methoxyethoxy)-4-(5-(4-methoxyphenyl)pyrazol-3-yloxy)quinazoline,

and salts thereof.

13. (Amended) The method as claimed in claim 1 selected from:

6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)-4-(5-phenylpyrazol-3-ylamino)-quinazoline

and

6,7-dimethoxy-4-(5-phenylpyrazol-3-ylloxy)quinazoline

and pharmaceutically acceptable salts thereof.

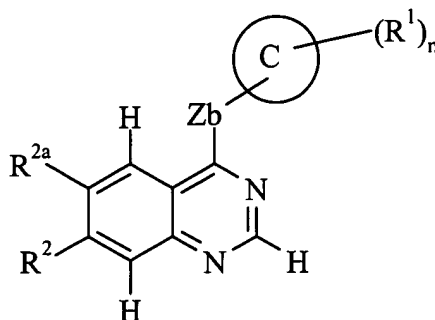
14. (Amended) A compound as claimed in any one of claims 18 and 5 to 12 in the form of a pharmaceutically acceptable salt.

16. (Amended) A pharmaceutical composition which comprises as active ingredient a compound of formula II or a pharmaceutically acceptable salt thereof as claimed in any one of claims 18 and 5 to 12 in association with a pharmaceutically acceptable excipient or carrier.

17. (Amended) A method for producing an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal in need of such treatment which comprises administering to said animal an effective amount of a compound of formula II as defined in any one of claims 18 and 5 to 12 or a pharmaceutically acceptable salt thereof.

Please cancel claim 4, without prejudice, and replace the subject matter thereof with new claim 18 as follows:

18. (New) A compound of the formula II:



wherein:

ring C is a 5-6-membered heterocyclic moiety which may be saturated or unsaturated, which may be aromatic or non-aromatic, and which contains 1-3 heteroatoms selected independently from O, N and S;

Zb is -O- or -S-;

R¹ represents hydrogen, C₁₋₄alkyl, C₁₋₄alkoxymethyl, di(C₁₋₄alkoxy)methyl, C₁₋₄alkanoyl, trifluoromethyl, cyano, amino, C₂₋₅alkenyl, C₂₋₅alkynyl, a phenyl group, a benzyl group or a 5-6-membered heterocyclic group with 1-3 heteroatoms, selected independently from O, S and N, which heterocyclic group may be aromatic or non-aromatic and may be saturated (linked via a ring carbon or nitrogen atom) or unsaturated (linked via a ring carbon atom), and which phenyl, benzyl or heterocyclic group may bear on one or more ring carbon atoms up to 5 substituents selected from hydroxy, halogeno, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃alkanoyloxy, trifluoromethyl, cyano, amino, nitro, C₂₋₄alkanoyl, C₁₋₄alkanoylamino, C₁₋₄alkoxycarbonyl, C₁₋₄alkylsulphanyl, C₁₋₄alkylsulphinyl, C₁₋₄alkylsulphonyl, carbamoyl, N-C₁₋₄alkylcarbamoyl, N,N-di(C₁₋₄alkyl)carbamoyl, aminosulphonyl, N-C₁₋₄alkylaminosulphonyl, N,N-di(C₁₋₄alkyl)aminosulphonyl, C₁₋₄alkylsulphonylamino, C₁₋₄alkylamino, C₁₋₄hydroxyalkyl, C₁₋₄aminoalkyl, C₁₋₄haloalkyl, C₁₋₄hydroxyalkoxy, carboxy and a saturated heterocyclic group selected from morpholino, thiomorpholino, pyrrolidinyl, piperazinyl, piperidinyl imidazolidinyl and pyrazolidinyl, which saturated heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃alkanoyloxy, trifluoromethyl, cyano, amino, nitro and C₁₋₄alkoxycarbonyl; and additionally R¹ may

represent carboxy, C₃₋₇cycloalkyl, C₃₋₇cycloalkylC₁₋₃alkyl, or phenylC₂₋₄alkyl wherein the phenyl moiety may bear up to 5 substituents selected from the list herein defined for a phenyl ring which is directly linked to ring C;

n is an integer from 0 to 5;

m is an integer from 0 to 3;

R² represents hydroxy, cyano, nitro, trifluoromethyl, C₁₋₃alkylsulphanyl, -NR³R⁴ (wherein R³ and R⁴, which may be the same or different, each represents hydrogen or C₁₋₃alkyl), or R⁵X¹ (wherein X¹ represents a direct bond, -O-, -CH₂-, -OCO-, carbonyl, -S-, -SO-, -SO₂-, -NR⁶CO-, -CONR⁷-, -SO₂NR⁸-, -NR⁹SO₂- or -NR¹⁰- (wherein R⁶, R⁷, R⁸, R⁹ and R¹⁰ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl), and R⁵ is selected from one of the following eighteen groups:

- 1) hydrogen or C₁₋₅alkyl which may be unsubstituted or which may be substituted with one or more groups selected from hydroxy, fluoro, chloro, bromo and amino;
- 2) C₁₋₅alkylX²COR¹¹ (wherein X² represents -O- or -NR¹²- (in which R¹² represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R¹¹ represents C₁₋₃alkyl, -NR¹³R¹⁴ or -OR¹⁵ (wherein R¹³, R¹⁴ and R¹⁵ which may be the same or different each represents hydrogen, C₁₋₃alkyl, C₄₋₅alkyl or C₁₋₃alkoxyC₂₋₃alkyl));
- 3) C₁₋₅alkylX³R¹⁶ (wherein X³ represents -O-, -S-, -SO-, -SO₂-, -OCO-, -NR¹⁷CO-, -CONR¹⁸-, -SO₂NR¹⁹-, -NR²⁰SO₂- or -NR²¹- (wherein R¹⁷, R¹⁸, R¹⁹, R²⁰ and R²¹ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R¹⁶ represents hydrogen, C₁₋₃alkyl, cyclopentyl, cyclohexyl or a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C₁₋₃alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and C₁₋₄alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₄alkyl, C₁₋₄hydroxyalkyl, C₁₋₄alkoxy, C₁₋₄cyanoalkyl and C₁₋₄alkoxycarbonyl);
- 4) C₁₋₅alkylX⁴C₁₋₅alkylX⁵R²² (wherein X⁴ and X⁵ which may be the same or different are each -O-, -S-, -SO-, -SO₂-, -NR²³CO-, -CONR²⁴-, -SO₂NR²⁵-, -NR²⁶SO₂- or -NR²⁷- (wherein R²³, R²⁴, R²⁵, R²⁶ and R²⁷ each independently represents hydrogen, C₁₋₃alkyl

- or C₁₋₃alkoxyC₂₋₃alkyl) and R²² represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl);
- 5) R²⁸ (wherein R²⁸ is a 5-6-membered saturated heterocyclic group (linked via carbon or nitrogen) with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₄alkyl, C₁₋₄hydroxyalkyl, C₁₋₄alkoxy, C₁₋₄alkoxyC₁₋₄alkyl, C₁₋₄alkylsulphonylC₁₋₄alkyl and C₁₋₄alkoxycarbonyl);
- 6) C₁₋₅alkylR²⁸ (wherein R²⁸ is as defined herein);
- 7) C₂₋₅alkenylR²⁸ (wherein R²⁸ is as defined herein);
- 8) C₂₋₅alkynylR²⁸ (wherein R²⁸ is as defined herein);
- 9) R²⁹ (wherein R²⁹ represents a pyridone group, a phenyl group or a 5-6-membered aromatic heterocyclic group (linked via carbon or nitrogen) with 1-3 heteroatoms selected from O, N and S, which pyridone, phenyl or aromatic heterocyclic group may carry up to 5 substituents on an available carbon atom selected from hydroxy, halogeno, amino, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄hydroxyalkyl, C₁₋₄aminoalkyl, C₁₋₄alkylamino, C₁₋₄hydroxyalkoxy, carboxy, trifluoromethyl, cyano, -CONR³⁰R³¹ and -NR³²COR³³ (wherein R³⁰, R³¹, R³² and R³³, which may be the same or different, each represents hydrogen, C₁₋₄alkyl or C₁₋₃alkoxyC₂₋₃alkyl));
- 10) C₁₋₅alkylR²⁹ (wherein R²⁹ is as defined herein);
- 11) C₂₋₅alkenylR²⁹ (wherein R²⁹ is as defined herein);
- 12) C₂₋₅alkynylR²⁹ (wherein R²⁹ is as defined herein);
- 13) C₁₋₅alkylX⁶R²⁹ (wherein X⁶ represents -O-, -S-, -SO-, -SO₂-, -NR³⁴CO-, -CONR³⁵-, -SO₂NR³⁶-, -NR³⁷SO₂- or -NR³⁸- (wherein R³⁴, R³⁵, R³⁶, R³⁷ and R³⁸ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R²⁹ is as defined herein);
- 14) C₂₋₅alkenylX⁷R²⁹ (wherein X⁷ represents -O-, -S-, -SO-, -SO₂-, -NR³⁹CO-, -CONR⁴⁰-, -SO₂NR⁴¹-, -NR⁴²SO₂- or -NR⁴³- (wherein R³⁹, R⁴⁰, R⁴¹, R⁴² and R⁴³ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R²⁹ is as defined herein);

15) C₂₋₅alkynylX⁸R²⁹ (wherein X⁸ represents -O-, -S-, -SO-, -SO₂-, -NR⁴⁴CO-, -CONR⁴⁵-, -SO₂NR⁴⁶-, -NR⁴⁷SO₂- or -NR⁴⁸- (wherein R⁴⁴, R⁴⁵, R⁴⁶, R⁴⁷ and R⁴⁸ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R²⁹ is as defined herein);

16) C₁₋₃alkylX⁹C₁₋₃alkylR²⁹ (wherein X⁹ represents -O-, -S-, -SO-, -SO₂-, -NR⁴⁹CO-, -CONR⁵⁰-, -SO₂NR⁵¹-, -NR⁵²SO₂- or -NR⁵³- (wherein R⁴⁹, R⁵⁰, R⁵¹, R⁵² and R⁵³ each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R²⁹ is as defined herein);

17) C₁₋₃alkylX⁹C₁₋₃alkylR²⁸ (wherein X⁹ and R²⁸ are as defined herein); and

18) C₁₋₃alkylR⁵⁴C₁₋₃alkylX⁹R⁵⁵ (wherein X⁹ is as defined herein and R⁵⁴ and R⁵⁵ are each independently selected from hydrogen, C₁₋₃alkyl, cyclopentyl, cyclohexyl and a 5-6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which C₁₋₃alkyl group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno and C₁₋₄alkoxy and which cyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₄alkyl, C₁₋₄hydroxyalkyl, C₁₋₄alkoxy, C₁₋₄cyanoalkyl and C₁₋₄alkoxycarbonyl), with the proviso that R⁵⁴ cannot be hydrogen;

and additionally wherein any C₁₋₅alkyl, C₂₋₅alkenyl or C₂₋₅alkynyl group in R⁵X¹- may bear one or more substituents selected from hydroxy, halogeno and amino; provided that R² is not hydrogen, substituted or unsubstituted C₁₋₅alkyl, C₁₋₅alkoxy, phenoxy or phenylC₁₋₅alkoxy; and

R^{2a} represents hydrogen, halogeno, C₁₋₃alkyl, C₁₋₃alkoxy, C₁₋₃alkylthio, -NR^{3a}R^{4a} (wherein R^{3a} and R^{4a}, which may be the same or different, each represents hydrogen or C₁₋₃alkyl), or R^{5a}(CH₂)_{za}X^{1a} (wherein R^{5a} is a 5- or 6-membered saturated heterocyclic group with 1-2 heteroatoms, selected independently from O, S and N, which heterocyclic group may bear 1 or 2 substituents selected from oxo, hydroxy, halogeno, C₁₋₄alkyl, C₁₋₄hydroxyalkyl and C₁₋₄alkoxy, za is an integer from 0 to 4 and X^{1a} represents a direct bond, -O-, -CH₂-, -S-, -SO-, -SO₂-, -NR^{6a}CO-, -CONR^{7a}-, -SO₂NR^{8a}-, -NR^{9a}SO₂- or

Sub
C2

BS

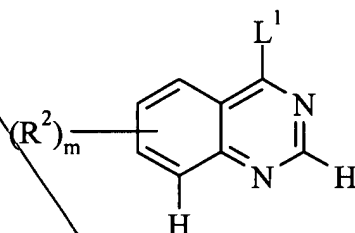
-NR^{10a} - (wherein R^{6a}, R^{7a}, R^{8a}, R^{9a} and R^{10a} each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl));

or a salt thereof.

Please cancel claim 15, without prejudice, and replace the subject matter thereof with new claim 19 as follows:

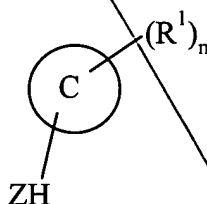
19. (New) A process for the preparation of a compound of formula II or salt thereof, as defined in claim 18, which comprises:

(a) the reaction of a compound of the formula III:



(III)

(wherein R² and m are as defined in claim 18 and L¹ is a displaceable moiety), with a compound of the formula IV:

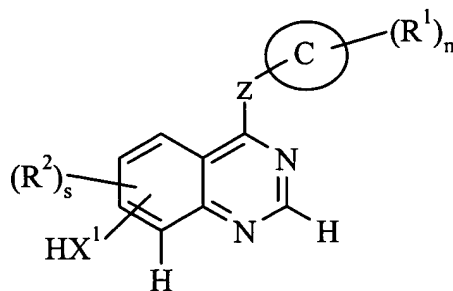


(IV)

(wherein ring C, R¹, Z and n are as defined in claim 18);

BS
Sub
C2

- (b) compounds of formula II and salts thereof wherein at least one R^2 is R^5X^1 wherein R^5 is as defined in claim 18 and X^1 is -O-, -S-, -OCO- or -NR¹⁰- (wherein R^{10} independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) may be prepared by the reaction of a compound of the formula V:



(V)

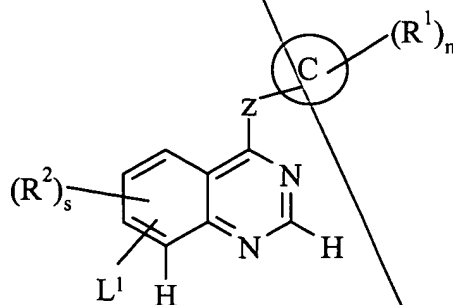
(wherein ring C, Z, R^1 , R^2 and n are as defined in claim 18 and X^1 is as defined herein in this section and s is an integer from 0 to 2) with a compound of formula VI:



(VI)

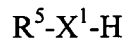
(wherein R^5 is as defined in claim 18 and L^1 is as defined herein);

- (c) compounds of the formula II and salts thereof wherein at least one R^2 is R^5X^1 wherein R^5 is as defined in claim 18 and X^1 is -O-, -S-, -OCO- or -NR¹⁰- (wherein R^{10} represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) may be prepared by the reaction of a compound of the formula VII:



(VII)

with a compound of the formula VIII:



(VIII)

(wherein R^1 , R^2 , R^5 , ring C, Z and n are as defined in claim 18 and s and L^1 are as defined herein and X^1 is as defined herein in this section);

(d) compounds of the formula II and salts thereof wherein at least one R^2 is R^5X^1 wherein X^1 is as defined in claim 18 and R^5 is $C_{1-5}alkylR^{62}$, wherein R^{62} is selected from one of the following nine groups:

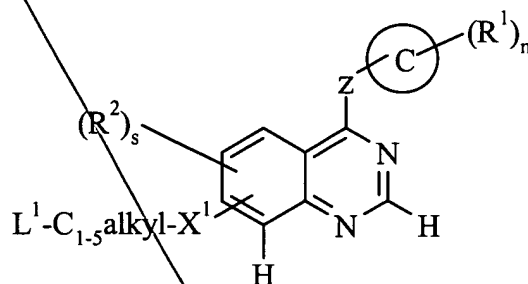
- 1) $X^{10}C_{1-3}alkyl$ (wherein X^{10} represents -O-, -S-, -SO₂-, -NR⁶³CO- or -NR⁶⁴SO₂- (wherein R^{63} and R^{64} which may be the same or different are each hydrogen, $C_{1-3}alkyl$ or $C_{1-3}alkoxyC_{2-3}alkyl$);
- 2) NR⁶⁵R⁶⁶ (wherein R^{65} and R^{66} which may be the same or different are each hydrogen, $C_{1-3}alkyl$ or $C_{1-3}alkoxyC_{2-3}alkyl$);
- 3) $X^{11}C_{1-5}alkylX^5R^{22}$ (wherein X^{11} represents -O-, -S-, -SO₂-, -NR⁶⁷CO-, -NR⁶⁸SO₂- or -NR⁶⁹- (wherein R^{67} , R^{68} , and R^{69} which may be the same or different are each hydrogen, $C_{1-3}alkyl$ or $C_{1-3}alkoxyC_{2-3}alkyl$) and X^5 and R^{22} are as defined in claim 18);
- 4) R^{28} (wherein R^{28} is as defined in claim 18);
- 5) $X^{12}R^{29}$ (wherein X^{12} represents -O-, -S-, -SO₂-, -NR⁷⁰CO-, -NR⁷¹SO₂-, or -NR⁷²- (wherein R^{70} , R^{71} , and R^{72} which may be the same or different are each hydrogen, $C_{1-3}alkyl$ or $C_{1-3}alkoxyC_{2-3}alkyl$) and R^{29} is as defined in claim 18);
- 6) $X^{13}C_{1-5}alkylR^{29}$, preferably $X^{13}C_{1-3}alkylR^{29}$, (wherein X^{13} represents -O-, -S-, -SO₂-, -NR⁷³CO-, -NR⁷⁴SO₂- or -NR⁷⁵- (wherein R^{73} , R^{74} and R^{75} each independently represents hydrogen, $C_{1-3}alkyl$ or $C_{1-3}alkoxyC_{2-3}alkyl$) and R^{29} is as defined in claim 18);

7) R^{29} (wherein R^{29} is as defined in claim 18);

8) $X^{14}C_{1-3}alkylR^{28}$ (wherein X^{14} represents -O-, -S-, -SO₂-, -NR⁷⁶CO-, -NR⁷⁷SO₂- or -NR⁷⁸- (wherein R^{76} , R^{77} and R^{78} each independently represents hydrogen, C₁₋₃alkyl or C₁₋₃alkoxyC₂₋₃alkyl) and R^{28} is as defined in claim 18); and

9) $R^{54}C_{1-3}alkylX^9R^{55}$ (wherein R^{54} , R^{55} and X^9 are as defined in claim 18);

may be prepared by reacting a compound of the formula IX:



(IX)

(wherein X^1 , R^1 , R^2 , ring C, Z and n are as defined in claim 18 and s and L^1 are as defined herein) with a compound of the formula X:



(X)

(wherein R^{62} is as defined herein);

(e) compounds of the formula II and salts thereof wherein one or more of the substituents $(R^2)_m$ is represented by -NR⁷⁹R⁸⁰, where one (and the other is hydrogen) or both of R^{79} and R^{80} are C₁₋₃alkyl, may be prepared by the reaction of compounds of formula II wherein the substituent $(R^2)_m$ is an amino group and an alkylating agent;

(f) compounds of the formula II and salts thereof wherein X^1 is -SO- or -SO₂- may be prepared by oxidation from the corresponding compound in which X^1 is -S- or -SO-; and when a salt of a compound of formula II is required, reaction of the compound obtained with an acid or base whereby to obtain the desired salt.